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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

4107-10m

MEMORANDUM

SUBJECT: PP#2E4051. Difenoconazole (**Dividend**) in Imported Wheat, ~~Barley,~~ and Rye Grain. Amendment of 1/6/93. MRID#s 428065-01c, -02c, -04 & -05. Barcode D195157. Case 283001. CBTS# 12585.

FROM: G.F. Kramer Ph.D., Chemist
Tolerance Petition Section III
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

THRU: P.V. Errico, Section Head
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

TO: Cynthia Giles-Parker, Product Manager
James Stone, Team 22 Reviewer
Registration Division (7505C)

CIBA-GEIGY Corporation proposes import tolerances for residues of the fungicide difenoconazole (1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole) of 0.1 ppm on wheat, barley, and rye grains as the result of seed treatment. The current amendment addresses deficiencies identified in CBTS' previous review (Memo R. Lascola 10/26/92).

In the Detailed Considerations section of this Memo, the outstanding deficiencies which apply to import tolerances, listed as presented in the Memo of R. Lascola (10/26/92), are followed by the petitioner's response and our conclusions.

RECOMMENDATIONS

CBTS continues to recommend against the proposed imported tolerances of 0.1 ppm for difenoconazole on wheat, barley, and rye

grains for the reasons outlined in Conclusions 1 and 4. The registrant must submit a CSF for Dividend 3SF and assure us that this product does not have foreign registration for foliar use on wheat, barley and rye.

CONCLUSIONS

1. With the exception of a CSF for Dividend 3SF, all requested product chemistry data has been provided by the registrant.

2. The registrant has submitted a copy of the analytical enforcement method which includes the recommendations made by ACL.

3. The petitioner has demonstrated that interferences from other pesticides registered for use on cereal grains will not occur with the analytical enforcement method.

4. The registrant has not assured us that there are no foreign foliar uses of difenoconazole on grains so that we can determine whether feeding studies and import tolerances on animal RACs are required. The registrant should provide this information.

Note to PM: When this tolerance is established, it should be as [(2S,4R)/(2R,4S)]/[(2R,4R)/(2S,4S)]1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole.

DETAILED CONSIDERATIONS

Deficiency - Conclusion 1a (from Memo, R. Lascola 10/26/92)

1a) The petitioner should specifically state whether their technical is a racemic mixture or is enriched with one or more enantiomers.

Petitioner's Response: The TGAI is a racemic mixture.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1b (from Memo, R. Lascola 10/26/92)

1b) The petitioner should revise the Confidential Statement of Formula for the technical product to include the CAS number for the active ingredient(s), and if necessary provide a new EPA Form 8570-4 which lists the fungicidally active enantiomers separate from the fungicidally inactive enantiomers. The latter should be listed as impurities. In addition, the petitioner should indicate if the CSF for the end-use product is appropriate for the **Dividend 150SF** or **3SF**

formulation. If different CSFs are appropriate for the two formulations, the petitioner should submit both.

Petitioner's Response: The CSF was revised to include the CAS number as well as the ratio of isomers. All enantiomers have approximately equivalent pesticidal activity. The CSF was also corrected to show a nominal value of 95% for the a.i. The original CSF mistakenly gave the lower limit, 92%, as the nominal.

CBTS' Conclusion: A new CSF for the TGAI has been provided by the registrant. The submitted form 8570-4 for technical difenoconazole includes the CAS#, the ratio of isomers and the correct nominal concentration of the a.i. Also, the registrant submitted a CSF for the Dividend 150SF formulation but did not submit a CSF for the 3SF formulation. **In order to completely resolve this deficiency, the registrant must submit a CSF for Dividend 3SF.**

Deficiency - Conclusion 1c (from Memo, R. Lascola 10/26/92)

1c) The petitioner should indicate the reaction time of Steps 1 and 2 of the manufacturing process.

Petitioner's Response: See the Confidential Appendix.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1d (from Memo, R. Lascola 10/26/92)

1d) The petitioner should indicate if nitrosamine formation is possible by any route other than decomposition of starting material.

Petitioner's Response: See the Confidential Appendix.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1e (from Memo, R. Lascola 10/26/92)

1e) The petitioner has included a method for determination of the cis/trans ratio of the parent compound, CGA-169374 (see below). However, nowhere is the actual ratio discussed. The petitioner must submit information for the five batches concerning the cis/trans ratio of the active ingredient, as well as any information available concerning the relative activities of the two isomers. Also, the petitioner should provide the chemical name of the technical product using the (RS) notation.

Petitioner's Response: See the Confidential Appendix.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved. The registrant has provided the

name of the a.i. in the CSF as [(2S,4R)/(2R,4S)]/[(2R,4R)/(2S,4S)] 1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1*H*-1,2,4-triazole.

Deficiency - Conclusion 1i (from Memo, R. Lascola 10/26/92)

1i) For Method AG-20/1, the petitioner should submit the results of an analysis of the technical product for nitrosamines for our review.

Petitioner's Response: This method was used to analyze the TGAI during the five-batch analysis. The level of nitrosamines was <0.5 ppm in all batches.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 1k (from Memo, R. Lascola 10/26/92)

1k) The petitioner should also refer to p. 10 of the Confidential Appendix for further comments about the validation of the analytical method for several impurities.

Petitioner's Response: See the Confidential Appendix.

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 5a (from Memo, R. Lascola 10/26/92)

5a) CBTS will withhold its conclusions concerning the suitability of Method AG-575 for enforcement purposes pending completion of the method validation trial as discussed in Conclusion 5c.

Results of PMV: This method, as submitted, is suitable for use as an enforcement method for the purposes of this petition for import tolerances on wheat, barley and rye grains. For future petitions on wheat, barley and rye straw and forages, the petitioner should amend the method to allow for use of a DB-17 megabore column instead of a packed column (Memo R. Lascola 12/28/92).

Petitioner's Response: Submission of:

> Difenoconazole (CGA-169374) Analytical Method for the Determination of CGA-169374 in Wheat RACs by GC with N/P Detection. Method AG-575B. MRID# 428065-04

CBTS' Conclusion: The revised method is amended to allow for use of a DB-17 megabore column. The PMV report is included as an appendix and is referenced in the body of the method as providing an alternative chromatographic procedure. This deficiency is now

resolved.

Deficiency - Conclusion 5b (from Memo, R. Lascola 10/26/92)

5b) The petitioner must demonstrate that interferences from other pesticides registered for use on cereal grains will not occur with this method.

Petitioner's Response: Submission of:

> Difenoconazole (CGA-169374) Specificity of Analytical Method AG-575A for the Determination of CGA-169374 in Small Grains. MRID# 428065-05

CBTS' Conclusion: Analytical samples were prepared as follows: nontreated wheat grain, wheat grain fortified with difenoconazole at levels of 0.01 and 0.10 ppm and five wheat grain samples each fortified with 12 different pesticides (registered for use on wheat, barley and/or rye) at the maximum tolerance level. Table 1 lists the pesticides tested (copied from p. 41-42 of MRID# 428065-05). These samples were analyzed by the analytical enforcement method. The recovery in the difenoconazole fortified samples was 116-121%. No interferant peak (<0.01 ppm) was observed in any of the samples containing the other pesticides. There were eight pesticides registered for use on wheat which were not tested. Zineb, inorganic bromides, CaCN, HCN, maneb and dinoseb were not used as salts would not be extractable from the aqueous phase; aluminum phosphide, as phosphine forms during extraction and is lost by evaporation; and Busan 72, as it is no longer available. These results demonstrate that Method AG-575A is specific for difenoconazole residues in wheat grain. The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 8 (from Memo, R. Lascola 10/26/92)

8) The petitioner has not submitted any animal feeding studies. However, based on the low residue levels resulting from the seed treatment use, CBTS concludes that tolerances on animal commodities are not necessary at this time. This evaluation will have to be reconsidered if additional uses and tolerances are proposed for CGA-169374 on animal feed commodities. The petitioner must assure us that this product will not be registered overseas for foliar use. If such a use is or will be registered, CBTS will require proposed meat (except poultry) and milk tolerances, appropriate analytical methodology, and animals feeding studies.

Petitioner's Response: None

CBTS' Conclusion: The requested information has <u>not</u> been provided. Ciba-Geigy has indicated that they have at least one registered foreign use with foliar applications (Memo R. Lascola 1/25/93). Specific details were not discussed. The registrant must provide the information on whether there are registered foreign foliar uses

of difenoconazole on cereal grains. As stated previously, if there are registered foreign foliar uses, CBTS will require proposed meat (except poultry) and milk tolerances, appropriate analytical methodology, and animal feeding studies. **This deficiency remains outstanding.**

cc (without Confidential Appendix):circ
cc (with Confidential Appendix): PP#2E4051, Kramer, circ., R.F.
RDI: P.V. Errico (1/3/94), R.A. Loranger (1/4/94), D.F Edwards (1/5/94)
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USER\CB:difenoco.003

TABLE I

COMPOUND	40 CFR 180	TOLERANCES (ppm)[3] BARLEY	RYE	WHEAT	MAXIMUM TOLERANCE[2]	sg added
GROUP 1						
1) Demeton	.105	0.75	—	0.75	0.75	11.25
2) Diuron	.106	1.0	1.0	1.0	1.0	15
3) Malathion	.111	8	8	8	8	120
4) Allethrin	.113	2	2	2	2	30
5) Methoxychlor	.120	2	2	2	2	30
6) Parathion	.121	1	0.5	1	1	15
7) Piperonyl Butoxide	.127	20	20	20	20	300
8) Pyrethrins	.128	3	3	3	3	45
9) Lindane	.133	0.1	0.1	0.1	0.1	1.5
10) Toxaphene	.138	5	5	5	5	75
11) 2,4-D	.142	0.5	0.5	0.5	0.5	7.5
12) Dalapon	.150	—	—	2	2	30
GROUP 2						
13) Azinphosmethyl	.154	0.2	0.2	0.2	0.2	3
14) Carbaryl	.169	0.2	0.2	3	3	45
15) Endosulfan	.182	0.1	0.1	0.1	0.1	1.5
16) Dinitrocresol	.183	0.75	—	0.3	0.75	11.25
17) Linuron	.184	0.25	0.25	0.25	0.25	3.75
18) Trichlorfon	.198	0.1	—	0.1	0.1	1.5
19) Dinoseb	.204	—	—	0.04	0.04	0.60
20) Paraquat Dichloride	.205	0.05	0.05	0.05	0.05	0.75
21) Fluoride	.206	0.1	—	0.05	0.1	1.5
22) Trifluralin	.207	—	—	0.05	0.05	0.75
23) Asulam	.220	—	—	0.25	0.25	3.75
24) Dicamba	.227	0.5	—	0.5	0.5	7.5
GROUP 3						
25) Thiabendazole	.242	—	—	1	1	15
26) Methomyl	.253	1	1	1	1	15
27) Carbofuran	.254	0.2	—	0.2	0.2	3
28) Terbacyn	.265	0.1	—	0.1	0.1	1.5
29) Barban	.268	0.1	—	0.1	0.1	1.5
30) Propanil	.274	0.2	—	0.2	0.2	3
31) Di-Allate	.277	0.05	—	—	0.05	0.75
32) Fluridone	.292	0.5	—	0.5	0.5	7.5
33) Benomyl	.294	0.2	0.2	0.2	0.2	3
34) Bitertan	.300	2	—	2	2	30
35) Carboxin	.301	0.2	—	0.2	0.2	3
36) Oryzalin	.304	0.05	—	0.05	0.05	0.75

TABLE I
(Continued)

COMPOUND	40 CFR 180	TOLERANCES (ppm) BARLEY	RYE	WHEAT	MAXIMUM TOLERANCE	as added
GROUP 4						
37) Cyanazine	307	—	—	0.1	0.1	1.5
38) Tri-Allate	314	0.05	—	0.05	0.05	0.75
39) Propham	319	—	—	0.1	0.1	1.5
40) Bromoxynil	324	0.1	0.1	0.1	0.1	1.5
41) Metribuzin	332	0.75	—	0.75	0.75	11.25
42) MCPA	339	0.1	0.1	0.1	0.1	1.5
43) Nitrapyrin	350	—	—	0.1	0.1	1.5
44) Bifenox	351	0.05	—	0.05	0.05	0.75
45) Metolachlor	368	0.1	0.1	0.1	0.1	1.5
46) Difenzoquat	369	0.2	—	0.05	0.2	3
47) Terrazole	370	—	—	0.05	0.05	0.75
48) Thiophanate Methyl	371	—	—	0.05	0.05	0.75
GROUP 5						
49) Diclofop-Methyl	385	0.1	—	0.1	0.1	1.5
50) Chlorsulfuron	405	0.1	—	0.1	0.1	1.5
51) Metalaxyl	408	0.2	—	0.2	0.2	3
52) Triadimefon	410	1	—	1	1	15
53) Imazalil	413	0.05	—	0.05	0.05	0.75
54) Chlorpyrifos-Methyl	419	6	—	6	6	90
55) Metsulfuron-Methyl	428	0.05	—	0.05	0.05	0.75
56) Clopyralid	431	3	—	3	3	45
57) Propiconazole	434	0.1	0.1	0.1	0.1	1.5
58) Thifensulfuron	439	0.05	—	0.05	0.05	0.75
59) Tridimenol	450	0.05	0.05	0.05	0.05	0.75
60) Tribenuron-Methyl	451	0.05	—	0.05	0.05	0.75

Confidential Appendix to PP#2E4051

(CBTS# 12585)

Pages 10-11 – *Manufacturing process information may be entitled to confidential treatment*

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